UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Office of Prevention, Pesticides
and Toxic Substances

5/5/00

MEMORANDUM

SUBJECT: Sodium Acifluorfen (PC Code: 114402): HED Metabolism Assessment Review Committee Decision Document (DP Barcode: D265602).

FROM: William J. Hazel, Ph.D., Chemist
Reregistration Branch 1
Health Effects Division (7509 C)

THRU: Whang Phang, Ph.D., Senior Scientist
Reregistration Branch 1
Health Effects Division (7509 C)

and

Christine L. Olinger, Executive Secretary
Metabolism Assessment Review Committee
Health Effects Division (7509 C)

TO: George F. Kramer, Ph.D., Executive Secretary
Metabolism Assessment Review Committee
Health Effects Division (7509 C)

ATTENDEES

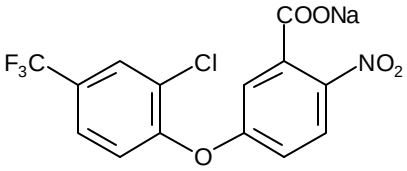
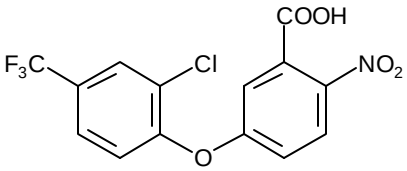
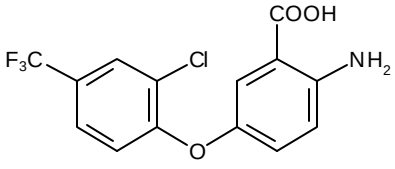
MARC members: George Kramer, Christine Olinger, Elizabeth Mendez, John Doherty, Nancy Dodd, Leung Cheng, Alberto Protzel, Kit Farwell

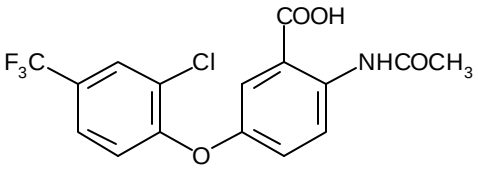
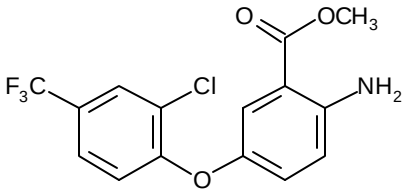
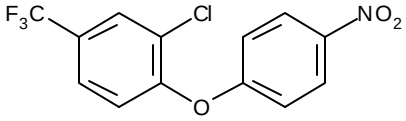
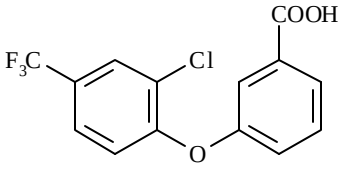
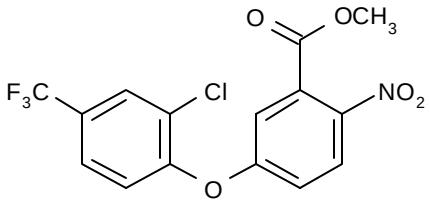
Other attendees: William Hazel, James Wolf, Paul Chin, Christina Scheltema

SUMMARY OF DELIBERATIONS

HED's Metabolism Assessment Review Committee (MARC) met 4/4/00 to discuss the results of **sodium acifluorfen** plant and livestock metabolism studies and to address the issues raised in the 3/14/00 request for MARC consideration prepared by W. Hazel (D264044). Analytical methodology, rotational crop data, and relevant magnitude of the residue in plants, toxicology, and soil/water information were also discussed as needed. The MARC was requested to provide recommendations regarding the sodium acifluorfen residues of toxicological and regulatory concern in both plants and animals. Available metabolism studies upon which this request is based include peanut, rice, soybean, hen, and goat. The current tolerances are established at 40 CFR 180.383 and include sodium acifluorfen, acifluorfen acid, the methyl ester of the acid, and the amino analogs of these. The structures of these and other potential residues of concern are presented in Table 1. Note that structures I, II, III, V, and VIII are currently included in the tolerance expression.

Table 1. Sodium acifluorfen and its metabolites.

Code	Chemical Name / Structure	Substrate / **Common Name**
I.	Sodium 5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-nitrobenzoate 	**Sodium acifluorfen**
II.	5-[2-Chloro-4-(trifluoromethyl)-phenoxy]-2-nitrobenzoic acid 	goat milk, fat, kidney, liver, and muscle; hen egg white, yolk, fat, liver, and muscle; peanut seed, hulls, and vines; rice grain, forage, straw **Acifluorfen**
III.	5-[2-Chloro-4-(trifluoromethyl)-phenoxy]-2-aminobenzoic acid 	goat milk, fat, kidney, liver, and muscle; peanut seed, hulls, and vines; rice grain and straw **Acifluorfen amino**
IV.	5-[2-Chloro-4-(trifluoromethyl)-phenoxy]-2-acetamidobenzoic acid	

Code	Chemical Name Structure	Substrate **Common Name**
		goat milk, fat, kidney, liver, and muscle; hen egg white, yolk, fat, liver, and muscle **Acifluorfen acetamide**
V.	Methyl 5-[2-chloro-4-(trifluoromethyl)-phenoxy]-2-aminobenzoate 	goat milk, fat, and muscle **Acifluorfen amino methyl ester**
VI.	4-(2-chloro-4-(trifluoromethyl)phenoxy)nitrobenzene 	hen egg white, egg yolk, fat, liver, and thigh muscle; peanut seed, hulls, and vines **Descarboxy acifluorfen**
VII.	3-(2-chloro-4-trifluoromethylphenoxy)benzoic acid 	peanut seed, hulls, and vines **Desnitro-acifluorfen**
VIII.	Methyl 5-[2-chloro-4-(trifluoromethyl)-phenoxy]-2-nitrobenzoate 	Not found in plants or animals; this is an analyte **Acifluorfen methyl ester**

DETAILED CONSIDERATIONS

Use Pattern

Acifluorfen is registered for use on peanut, rice, and soybean. There is a strawberry tolerance but there is no registered use on strawberry at this time. Acifluorfen products used on agricultural sites are all formulated as Soluble Concentrates (SC) containing 0.67-2 lb ai/gal. Postemergence broadcast applications are made by ground or air at 0.16-0.5 lb ai/A. PHIs are 50-90 days. No more than two applications are to be made per season. The seasonal maximum rate is 0.5 lb ai/A (IR-4 proposed 1.0 lb ai/A for strawberries). Of the sodium acifluorfen used annually, 93% is used on soybeans (9% crop treated = CT), 4% is used on peanuts (11% CT), and 2% is used on rice (4% CT).

U.S. Tolerances

The following tolerances have been established for residues of sodium acifluorfen, acifluorfen acid, acifluorfen amine, acifluorfen methyl ester, and acifluorfen amine methyl ester [40 CFR 180.393(a)]: 0.05 ppm in strawberry and 0.1 ppm in peanuts, rice grain and straw, and soybeans; animal commodity tolerances are 0.02 ppm in milk, eggs, poultry fat, meat byproducts, and meat, and the liver and kidney of cattle, goats, hogs, horses, and sheep. Time-limited Section 18 tolerances with expiration dates of 12/31/98 are listed under 40 CFR §180.383(b) for cowpeas, lima beans, and Southern peas at 0.1 ppm. Acifluorfen is also currently regulated as a metabolite of the herbicide lactofen under 40 CFR §180.432; note, however, that the MARC, also at this 4/4/00 meeting, determined that acifluorfen is not a significant plant metabolite of lactofen and that the residue definition at 180.432 should be revised to delete acifluorfen.

International Tolerances

No Codex MRLs or Canadian or Mexican tolerances have been established for residues of sodium acifluorfen in food or feed.

Qualitative Nature of the Residue in Lactating Goats

BASF Corporation submitted data (1993; MRID 42815601) depicting metabolism of uniformly [^{14}C] chlorophenyl ring-labeled sodium acifluorfen in a lactating goat. The test goat was orally dosed once a day for four consecutive days with 19.7 mg of [^{14}C]sodium acifluorfen [specific activity 8.67 mCi/mmole (22.6 FCi/mg or 50172 dpm/Fg)]. The dose of [^{14}C]sodium acifluorfen used in the study was equivalent to 10.1 ppm at a feed consumption of 1.95 kg/goat/day. This dosing level is ca. 150x the maximum dietary burden. The goats were sacrificed ca. 22 hours following the final dose.

The 5/12/94 (L. Cheng, D192655) review concluded that the goat metabolism study was

adequate. Acifluorfen, acifluorfen amino glucuronide, acifluorfen acetamide, acifluorfen amino, and acifluorfen amino methyl ester were identified in milk, fat, and muscle, and the same except acifluorfen amino methyl ester were identified in kidney and liver. Amounts of TRR that were identified were 55.3% in milk, 67.6% in fat, 59.5% in muscle, 84.8% in kidney, and 70.5% in liver. The remaining residue was analyzed on HPLC and none of the separated components exceeded 5% TRR or 0.01 ppm. No components resulting from the cleavage of the diphenylether bond were observed among the metabolites identified. CBRS waived the second goat metabolism study in which acifluorfen is labeled in the chlorophenyl ring (L. Cheng, 9/16/94, D206424).

Qualitative Nature of the Residue in Poultry

BASF Corporation (1993; MRID 42828201) submitted data depicting the metabolism of sodium acifluorfen that was labeled with [^{14}C] in the chlorophenyl ring (CPR) (specific activity, 18.03 mCi/mmole, 104,333.8 dpm/ug; 95-96% radiochemical purity) and in the nitrophenyl ring (NPR) (specific activity, 16.0 mCi/mmole, 92,586.8 dpm/ug; radiochemical purity 96%) in laying hens. Two groups of five white leghorn hens were orally dosed with CPR labeled sodium acifluorfen and NPR labeled sodium acifluorfen, once daily for 5 consecutive days at 11.1 ppm and 9.2 ppm, respectively. These doses are equivalent to 92x the maximum daily dietary burden for the CPR-labeled test substance and 111x for the NPR-labeled test substance. Hens were sacrificed 22-23 hours following the final dose.

The qualitative nature of the residue in poultry was determined to be adequately understood (L. Cheng, 4/25/94, D192899). No metabolites were identified that indicate cleavage of the diphenyl ether bond. Acifluorfen was a major residue in egg white (up to 40% of the total radioactive residue; TRR), egg yolk (up to 22%), liver (up to 11%), and thigh muscle (up to 18%). Acifluorfen acetamide accounted for up to 20% of the residue in egg white, 15% in liver, and 20% in thigh muscle. Descarboxy acifluorfen comprised up to 11% of the residue in egg white, 30% in egg yolk, 15% in liver, and 50% in thigh muscle. Descarboxy acifluorfen was the major residue in fat accounting for 50-70% of the residue.

The study successfully characterized/identified the following levels of radioactivity in matrices of hens orally dosed with CPR- and NPR-labeled acifluorfen: egg white (87.2-90.7% TRR), egg yolk (64.5-74.5% TRR), fat (89.9-98.5% TRR), liver (84.3-90.8% TRR), and thigh muscle (88.3-106.2% TRR).

Metabolism of [^{14}C]sodium acifluorfen in peanuts

BASF Corporation submitted data (1992; MRID 42368301) pertaining to the metabolism of [^{14}C]sodium acifluorfen in peanuts. Field-grown peanuts received two foliar applications of uniformly CF_3-ring-labeled [^{14}C]sodium acifluorfen (specific activity 8.005 µCi/mg, 3.071 mCi/mMol, 1.777 x 10^4 dpm/µg; radiochemical purity 98.3%) at a rate equivalent to 0.5 lb ai/A/application (1x the maximum registered single use rate). The first application was made when the plants were in bloom stage and the second 22 days following the first,

when the plants were in the early pegging stage.

The metabolism of sodium acifluorfen in peanuts is adequately understood (S. Knizner, 6/7/95, D205291). TRR in the mature plant were: 1.93 ppm in fodder, 0.717 ppm in hulls, and 0.181 ppm in seed. Residues in peanut seed and hulls were adequately identified/characterized and consist primarily of acifluorfen per se, conjugates (cysteine and thioglucoside) of the nitrobenzoic acid ring resulting from diphenyl ether cleavage, and polar metabolites. Residues identified in immature peanut commodities included acifluorfen, desnitroacifluorfen, and descarboxyacifluorfen.

In fodder, acifluorfen accounted for 13.2% TRR (0.0255 ppm) and "polar" components accounted for 33.1% TRR (0.642 ppm). The registrant stated that no further characterization of radioactive residues in fodder was performed because of the label restrictions prohibiting use of treated plants for feed or forage. Although initially rejected, this argument was later accepted when HED decided that feeding restrictions for peanut commodities are practical and the restrictions will be accepted.

In seed, acifluorfen was the major identified residue at 4.9% TRR (0.008 ppm). A total of 63.1% TRR was characterized as being polar in nature, consisting of numerous compounds (ranging from 0.3% to 16.2% TRR, <0.001 to 0.028 ppm). The PES contained 22.6% TRR (0.041 ppm) and was not analyzed further.

In hulls, acifluorfen was identified at 11.0% TRR (0.078 ppm). The thioglucoside conjugate of the nitrobenzoic acid ring, 3-carboxy-4-nitrophenyl thio-beta-D-glucopyranoside accounted for 26.3% TRR (0.189 ppm) and S-(3-carboxy-4-nitrophenyl)-cysteine accounted for 6.4% TRR (0.046 ppm). At least 15 polar components were present, all ≤3.6% TRR (≤0.026 ppm) for a total of 30.7% TRR (0.220 ppm).

Metabolism of [^{14}C]sodium acifluorfen in rice

BASF Corporation submitted data (1992; MRID 42368302) pertaining to the metabolism of sodium acifluorfen in rice. Greenhouse-grown rice plants that had been planted in three 55-gallon barrels received one "over-the-top" foliar application of uniformly CF_3-ring-labeled [^{14}C]sodium acifluorfen (specific activity 3.071 mCi/mMol, radiochemical purity 99.4%) when the plants were in the early boot stage of growth at a rate equivalent to 0.43 lb ai/A (3.4x the maximum registered single use rate or 1.7x the maximum seasonal use rate).

The metabolism of sodium acifluorfen in rice is adequately understood based on the following reviews, taken together: J. Abbotts, 12/2/92, D180455; F. Suhre, 5/3/94, D201623; and L. Cheng, 4/4/96, D222843. The organosoluble residues from the 0-day forage sample contained 89% acifluorfen. Acifluorfen represented 75% TRR in 7-day forage and 73% TRR in 40-day forage. In 97-day straw, 72% of the TRR was acifluorfen and 6% TRR was 2-chloro-4-trifluoromethylphenol. Therefore, some cleavage of the

diphenylether linkage results residues by the time the foliage matures and dries into straw following grain harvest. In grain, 31% of the TRR was acifluorfen and 68% was aminoacifluorfen. In hulls, 5-7% TRR was acifluorfen.

Metabolism of [^{14}C]sodium acifluorfen in soybeans

BASF submitted data (1994; MRID 43181901) pertaining to the metabolites of [^{14}C]acifluorfen in soybeans. Two applications of sodium [^{14}C]acifluorfen, uniformly ring labeled in the nitrobenzoic acid ring and formulated as a sodium salt, were made to soybeans at ~0.27 lb ai/A/application for a total application of 0.543 lb ai/A (1.09x the stated maximum use rate). The radiolabeled compound had a specific activity of 55,500 dpm/µg and a radiochemical purity of $94.5%. The foliar applications were made to field grown soybeans using a hand-held sprayer at 21 and 81 days after planting. The whole aerial portion of the immature soybean plants (forage) were sampled 2-3 hours after the first and second applications and 13 days after the second application. Mature soybean seeds and fodder (including empty pods) were sampled 50 days after the second application.

Acifluorfen metabolism in soybeans is considered to be adequate (W. Hazel, 5/4/00, D201621). Of the TRR, 20% and 82% was, respectively, identified and characterized in seed. Acifluorfen per se is the major residue identified in seed 50 days posttreatment at 8.9% of the TRR (0.043 ppm). In forage at 50 days, 27% and 53% of the TRR was identified and characterized, respectively. Similarly, in forage, acifluorfen is the major identified residue: 83% of the TRR on 0-day (28 ppm), 58% TRR on day 13 (16 ppm), and 27% TRR on day 50 (7 ppm). Smaller amounts of desnitro acifluorfen (0.4% TRR) and descarboxy acifluorfen (0.2 % TRR) were found in forage on days 0 and 13. Some cleavage of the diphenylether linkage occurs in seed by maturity as evidenced by the cysteine (6.4% TRR or 0.031 ppm) and thioglucoside (12% TRR or 0.059 ppm) conjugates of the nitrobenzoic acid moiety found after 50 days..

Are Residues Systemic?

Acifluorfen residues are absorbed through the both the leaves and the roots and are translocated throughout the plant.

ANALYTICAL METHODOLOGY

Analytical methods for tolerance enforcement are published in PAM, Vol. II. Sodium acifluorfen, the free acid, and the amine analog are all converted to their methyl esters by methylation with diazomethane. The amine methyl ester is then converted to its amide derivative with heptafluorobutyric anhydride. Analysis is by gas chromatography with electron capture detection; separate peaks are identified for derivatized compounds, the methyl ester and the amide. Limits of detection are 0.01 ppm for each compound. Phase 4 review concluded that methods in PAM, Vol. II are adequate for data collection and

tolerance enforcement, for the residues in the present tolerance expression.

The tolerance enforcement method in PAM II has not been radiovalidated. Acifluorfen and its metabolites are not recovered using FDA's Multiresidue Methods based on FDA's PestData (10/99). Conjugates are not determined by the data collection or enforcement methods.

ENVIRONMENTAL FATE/WATER ASSESSMENT OF ACIFLUORFEN

Parent sodium acifluorfen is stable to hydrolysis, and is extremely water soluble (2.50×10^5 ppm at 20.0°C). Acifluorfen is a relatively persistent chemical as indicated by the aerobic soil metabolism study ($t_{1/2}$= 108 - 200 days). In the aerobic aquatic study, acifluorfen was relatively stable decreasing from 89% TAR at day 0 to 81.8% TAR at day 35. A half-life of 117 days is estimated. An anaerobic soil metabolism study shows fairly rapid degradation giving a half-life of 30 days. In an anaerobic aquatic metabolism study, a half-life of 2.75 days was determined. The primary degradate under anaerobic conditions was the corresponding amine from the reduction of the nitro group (amino acifluorfen (5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-aminobenzoic acid). Amino acifluorfen averaged 64-71% of the amount applied at 25 through 375 days. In this and in an additional experiment in which samples were incubated under similar conditions for up to 375 days, the degradates, amino acifluorfen (5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-aminobenzoic acid), acifluorfen acetamide (5-[2-chloro-4-(trifluoromethyl)phenoxy]-2-acetamidobenzoic acid), and desnitro acifluorfen (3-[2-chloro-4-(trifluoromethyl)phenoxy]-benzoic acid) were identified in the soil:water systems. Little formation of $^{14}CO_2$ was observed in this system.

Sodium aciflourfen undergoes photolytic degradation in water with a half-life ranging from 21.7 hours to 352 hours depending on the pH and buffer systems used. In soils, acifluorfen is more photolytically stable. Photodegradation on soil is not considered a major degradation route in the environment for acifluorfen.

The unaged batch equilibrium study gives a strong indication of the high mobility of parent acifluorfen. Overall, the reviewed ground water studies as well as an earlier reviewed prospective study indicate that under certain conditions residues are able to leach through the soil profile and reach ground water.

When sodium acifluorfen reaches ground water the compound will persist indefinitely due to its stability to abiotic hydrolysis. During runoff events, sodium acifluorfen may reach surface waters from ground water where it would also persist for some time (unless there is some photodegradation; 3 to 4 day half-life). Sodium acifluorfen would not be expected to bioaccumulate in fish because of the low Kow value.

The following Health Advisories have been established for acifluorfen per se by EPA's Office of Water: for children, 2 ppb for 1- and 10-day exposures and 0.1 ppb for long-term exposure; adults, 0.4 ppb for long-term; and cancer (adult only?), 0.1 ppb at a 1/10,000 risk.

Qualitative Nature of the Residue in Rotational Crops

Only confined crop rotational studies are available. Total radioactive residues (TRR) were >0.01 ppm in leafy, root, and/or grain crops planted into soil that had been previously treated with sodium acifluorfen 39-370 days earlier. **The only residue identified was acifluorfen acid.** Many other more polar metabolites were present but none of these could be identified. Residues of acifluorfen were detected at: 0.011-0.024 ppb at 39- and 103-day PBIs; ≤0.004 ppm at 145- to 370-day PBIs. Note that 1-year plantback intervals (PBI) are recommended in the 5/5/00 Residue Chemistry Chapter of the RED for all crops except small grains for which a 6-month PBI is recommended.

SUMMARY OF RAT METABOLISM OF ACIFLUORFEN

Available metabolism data are adequate to satisfy the guideline requirements. With oral administration, acifluorfen was rapidly absorbed and eliminated mainly in the urine (46-58% of the dose) and feces (21-41% of the dose). The major component present in urine and feces was unchanged acifluorfen and amine metabolite, respectively. No tissue accumulation was observed.

In a rat metabolism study, Fischer 344 rats (5 animals/sex/group) received a single gavage dose of ^{14}C- or -^{13}C-ring-labeled acifluorfen at 16-17 or 116 mg/kg or daily oral dose of non-radioactive acifluorfen-sodium 10-12 mg/kg for 14 days followed by a single gavage dose of ^{14}C- or ^{13}C-ring-labeled acifluorfen at 10-12 mg/kg and an intravenous dosage at 11-15 mg/kg. The single low, single high, and multiple low oral dose studies indicate that acifluorfen is rapidly and almost completely absorbed into the systemic circulation and excreted in both the male and female rats within 4 days after dosing. Over a 4-day period, the radioactivity recovered in the urine and feces in male rats was 46-58% and 21-41% of the dose, respectively. In contrast, the radioactivity recovered in the urine and the feces in female animals was 60-82% and 5-23% of the dose, respectively. There was no indication of bioaccumulation in any tissue or organ after administration of each of the four dosage regimens. The major radioactive component present in blood (95-98%), urine (95%) and bile (93%) was unchanged acifluorfen. The major component in feces was the amine metabolite which accounted for 60-80% of the radioactivity. This study is classified as Acceptable/guideline and satisfied the guideline data requirement for a metabolism study (85-1) in rats.

In non-guideline mouse and rat metabolism studies, non-radioactive acifluorfen was given in the diet at levels of 1.5 mg/kg/day (for CD-1 mice only) and 54 mg/kg/day (for both CD-1 mice and Sprague-Dawley rats) for 28 days. On days 14 and 28 of the study, animals were given a single gavage dose of ^{14}C-acifluorfen at 1.5 mg/kg/day (2 female mice) and 54 mg/kg/day (2 male and female mice and 2 female rats). The dosages chosen for repeated dosing of non-radioactive acifluorfen were equivalent to the low-dose and high-dose in the mouse bioassay (1.5 and 54 mg/kg/day; 7.5 and 270 ppm) and high-dose in

the rat bioassay (54 mg/kg/day; 1080 ppm). Urine and feces were collected twice daily for two days and daily thereafter for 2 days. Practically the entire pulse dose of acifluorfen was excreted in the urine and feces within two to three days. Metabolites consisted mainly of free acid (RH-5781; 33-91% of the total dose), reduced amino form of RH-5781 (RH-4514; 11-38%), or origin material (6-35%) consisted of acid hydrolyzable conjugates of RH-5781 and RH-4514. This study is classified as Acceptable/non-guideline. It is acceptable for the purposes for which it was intended as a special study.

FQPA Safety Factor

The FQPA Safety Factor Committee determined that the 10X SF should be retained and applied to acute dietary risk assessments for females 13-50 and the infants and children subgroups; the SF applicable to the same population subgroups may be reduced to 3X for chronic dietary risk assessments (9/29/99 report).

QUESTIONS POSED TO THE MARC AND MARC RESPONSES:

Question 1. What are the residues to be regulated/of toxicological concern in plant commodities? The major identified residue, by far, is acifluorfen (acid). In rice grain, however, significant amounts of aminoacifluorfen occurs. None of the other currently-regulated residues appear to occur in plant commodities, at least at normal harvest time. Do we retain the currently regulated residues to guard against misuse and because the residue collection and enforcement methods pick them up?

MARC Response to Question 1. The residues to be regulated and of toxicological concern in plants will remain those in the current tolerance expression, i.e., the parent compound (sodium salt; not expected to be present), acifluorfen acid, acifluorfen amine, and the methyl esters of the acid and the amine. The MARC agreed that, although rarely found in plants, the two methyl esters should be included because: (i) there is no basis to exclude them due to toxicity; (ii) they are likely metabolites in plants and the amine methyl ester occurs in livestock; and (iii) because the data collection and enforcement methods convert other metabolites to these esters.

Question 2. In livestock, large amounts of several residues occur that are not currently regulated, namely acifluorfen acetamide, acifluorfen amino glucuronide, and descarboxyacifluorfen. The first two are conjugates that are not determined by the data collection or enforcement methods. Is the descarboxylated residue of toxicological concern at the levels seen? Should one or more of these be considered to be of toxicological concern and/or included in the tolerance expression? As the amino and amino methyl ester metabolites occur at fairly high levels in goats, it appears that the currently regulated residues are appropriate in livestock (although one or more may be added).

MARC Response to Question 2. The currently regulated residues should remain of toxicological concern and in the tolerance expression for livestock commodities, if tolerances are deemed necessary by the ChemSAC. In addition, should the feeding studies (if required) reveal that acifluorfen amino glucuronide, descarboxyacifluorfen, and acifluorfen acetamide are significant residues in livestock commodities, these metabolites should also be included as residues of concern for risk assessment purposes. The residue chemists are to determine whether these three additional metabolites need be included in the tolerance expression. Note that this will necessitate data collection/regulatory method development depending on the ChemSAC decision.

[Follow-up: On 5/3/00, ChemSAC determined that there is no reasonable expectation of finite residues transferring to livestock commodities from treated feed items based on the current use pattern. A weight-of-the-evidence approach was used to arrive at this decision (refer to the 5/3/00 ChemSAC minutes). Revocation of livestock tolerances, established at 0.02 ppm based on TRR levels from exaggerated feeding studies utilizing radiolabeled material, will be necessitated by this decision. In the event additional uses are registered in the future that result in finite acifluorfen residues in livestock commodities, acifluorfen amino glucuronide, descarboxyacifluorfen, and acifluorfen acetamide must be sought in livestock feeding studies, included in the dietary exposure estimates, and, if determined necessary, included in the tolerance expression.]

Question 3. Should livestock magnitude of the residue in ruminants (and poultry; see Question 4 below) be required based on the metabolism studies? If so, question 2 would be resolved by properly conducted feeding studies and by new method development.

MARC Response to Question 3. This question should be advanced to ChemSAC.

[Follow-up: See Follow-up associated with Question 2.]

Question 4. Do you agree that residues in poultry are Category 3 except for residues in fat?

MARC Response to Question 4. This question should be advanced to ChemSAC.

[Follow-up: See Follow-up associated with Question 2.]

Question 5. Is MARC concerned about the thioglucoside and cysteine conjugates of the nitrophenyl ring in peanut hulls at the levels found? This indicates cleavage of the diphenylether bond.

MARC Response to Question 5. These residues need not be included in the tolerance expression or for risk assessment because they are not expected to contribute to the toxicological effects induced by acifluorfen and its metabolites having the intact diphenylether bridge and because they occur only in peanut hulls, an insignificant feed item that is also not a human food.

OTHER MARC CONCLUSIONS:

1. As a 1-year plantback interval is proposed (6 months for small grains) and acifluorfen acid is the major residue in rotated crops, there is no basis to establish rotational crop tolerances. If needed in the future, the currently regulated plant residues would be appropriate.

2. The residues of concern to be used for the assessment of drinking water exposure and risk are acifluorfen and acifluorfen amine, the major soil/water residues. Note that, to date, EFED has modeled acifluorfen only.

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